UNIVERSITA' DI MESSINA
FACOLTA' DI SCIENZE

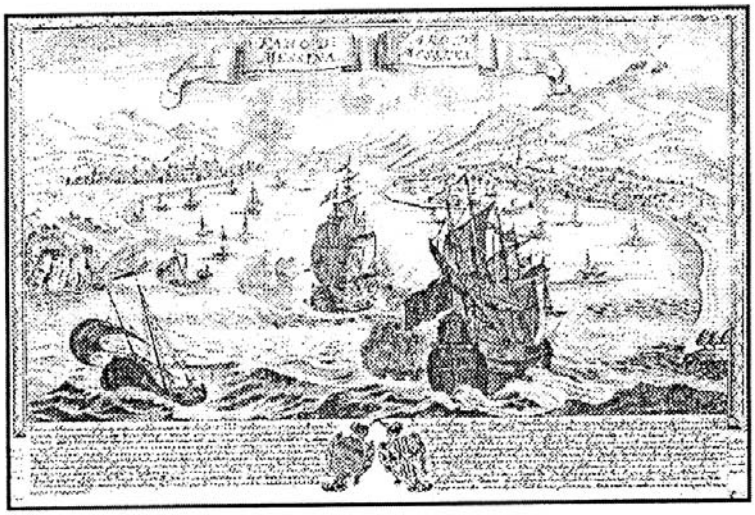
Dipartimento di Chimica Inorganica, Analititca
e Struttura Molecolare

Società Chimica Italiana
visione di Chimica Inorganica

Atti Accademia Peloritana dei Pericolanti
Classe I di Scienze Fisiche
Matematiche e Naturali

# WORKSHOP ON PLATINUM CHEMISTRY

# ABSTRACTS



MESSINA 30-31 MAGGIO 1994
Aula dell'Accademia

*Atti Accademia Peloritana dei Pericolanti*
*Classe I di Scienze Fis. Mat. e Na.*
*Vol. LXXII (1994) - Convegno 30-31 maggio 1994*

# STEREOSPECIFIC HYDROGEN BONDING IN PLATINUM NUCLEOTIDE INTERACTIONS

GIOVANNI NATILE

In DNA *cis*-DDP cross-links adjacent purine residues in a Head-to-Head (HH) conformation in which both the H8 atoms are on the same side of the platinum coordination plane. When the two nucleotide moieties are not linked by a phosphodiester group, the purines can have orientations in which the H8s are on opposite sides of the platinum coordination plane; this orientation is designated Head-to-Tail (HT) [1]. Normally only HT complexes are detected in solution and in most solid state crystallographic studies [2, 3]. The HH atropisomer, which is the best model for intrastrand binding of *cis*-platinum compounds to DNA, is difficult to isolate and has been found only in a crystal structure of *cis*-$[Pt(NH_3)_2(9\text{-ethyl-guanine})_2]X_2$ [4].

Investigation of complexes of the type $[Pt(5'GMP)_2$ $(R, S, S, R\text{-}Me_2DAB)]$ ($Me_2DAB$=N,N′-dimethyl-2,3-diamino-butane and the configurations at the four asymmetric centres are $R, S, S$, and $R$ at N, C, C, and N, respectively) has led to the first evidence for the existence of a HH atropisomer in solution [5]. In addition, the HH atropisomer is found to exist in equilibrium with two HT atropisomers, the predominant HT

having the Λ conformation. This is the first determination of the chirality of a HT species in solution; the ΔHT conformation had been found in all documented solid state structures for 6-oxopurine nucleot(s)ide complexes with metal centres [3].

The favoured HT atropisomer can form two O6-NH H-bonds, the HH atropisomer can form one O6-NH H-bond and the other HT atropisomer cannot form any O6-NH H-bond. Thus, O6-NH H-bond appears to dominate the stereochemistry of these complexes. For the complex with all asymmetric centres on $Me_2DAB$ inverted, [Pt(5′GMP)$_2$(*S*, *R*, *R*, *S*-$Me_2$DAB)], the dominant atropisomer has the ΔHT configuration. This result demonstrates that the stereochemistry of the ammine ligand influences the conformational equilibrium between atropisomers. The use of platinum(ll) complexes of stereochemically controlling ligands shows promise for controlling DNA or RNA conformations.

A similar investigation performed on the less symmetrical [Pt(5′GMP)$_2$-(*S*, *R*, *R*, *R*-$Me_2$DAB)] and [Pt(5′GMP)$_2$(*S*, *S*, *S*, *R*-$Me_2$DAB)] species has also demonstrated that both O6-NH and $ROPO_3$-NH H-bonds are important in determining the formed atropisomer [6].

The O6 can participate in H-bonding only when the O6 and the NH are on the same side of the coordination plane. When, instead, the H8 and the NH are on the same side, only phosphate group H-bonding is possible since in the normal anti conformation of 5′GMP, the phosphate group is close to H8 and hence to NH. Because the sugar moiety is flexible and there is relatively free rotation about the glycosyl bond, it is possible that a H-bond between the phosphate group and the NH is formed also when the H8 and NH are on opposite sides of the coordination plane. A quasi-equatorial NH is found to be particularly suitable to donate a strong hydrogen bond to the phosphate.

In conclusion modelling the stereochemistry of the NH atoms can lead to compounds with a strong preference for forming one type of adduct.

## REFERENCES

[1] R. E. Cramer, P. L. Dahlstrom, *Inorg. Chem.* **24** (1985) 3420.

[2] M. D. Reily, L. G. Marzilli, *J. Am. Chem. Soc.* **108** (1986,) 6785.

[3] B. Lippert, Prog. *Inorg. Chem.* **37** (1989) 1.

[4] B. Lippert, G. Raudaschl-Sieber, C. J. L. Lock, P. Pilon, *Inorg. Chim. Acta,* **93** (1984) 43. G. Schöllhorn, G. Raudaschl-Sieber, G. Müller, U. Thewalt, B. Lippert, *J. Am. Chem. Soc.* **107** (1985) 5932.

[5] Y. Xu, G. Natile, F. P. Intini, L. G. Marzilli, J. Am. Chem. Soc. **112** (1990) 8177.

[6] D. Kiser, F. P. Intini, Y. Xu, G. Natile, L. G. Marzilli, unpublished work.

*Dipartimento Farmaco-Chimico*
*via E. Orabona 4, 1-70125 Bari (Italy)*